

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

To:
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Date of mailing
(day/month/year)

10 AUG 2005

Applicant's or agent's file reference

DEX-0499

FOR FURTHER ACTION

See paragraph 2 below

International application No.

PCT/US05/10085

International filing date (day/month/year)

25 March 2005 (25.03.2005)

Priority date (day/month/year)

25 March 2004 (25.03.2004)

International Patent Classification (IPC) or both national classification and IPC

IPC(7): C07K 16/00; A61K 39/395; G01N 33/53 and US Cl.: 530; 387.1, 387.3, 388.1, 388.8; 424/130.1, 133.1, 141.1, 155.1; 435/7.1, 7.23

Applicant

DIADEXUS, INC.

1. This opinion contains indications relating to the following items:

- | | | |
|-------------------------------------|--------------|--|
| <input checked="" type="checkbox"/> | Box No. I | Basis of the opinion |
| <input type="checkbox"/> | Box No. II | Priority |
| <input type="checkbox"/> | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| <input type="checkbox"/> | Box No. IV | Lack of unity of invention |
| <input checked="" type="checkbox"/> | Box No. V | Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input type="checkbox"/> | Box No. VI | Certain documents cited |
| <input type="checkbox"/> | Box No. VII | Certain defects in the international application |
| <input checked="" type="checkbox"/> | Box No. VIII | Certain observations on the international application |

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US

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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/US05/10085

Box No. I Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

☒ a sequence listing

☐ table(s) related to the sequence listing

b. format of material

☒ in written format

☒ in computer readable form

c. time of filing/furnishing

☒ contained in international application as filed.

☒ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority for the purposes of search.

3. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

10/503799
IAP9 Rec'd PCT/PTO 21 SEP 2006

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

ISA/US03/10085

Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)

Claims Please See Continuation Sheet YES

Claims Please See Continuation Sheet NO

Inventive step (IS)

Claims Please See Continuation Sheet YES

Claims Please See Continuation Sheet NO

Industrial applicability (IA)

Claims Please See Continuation Sheet YES

Claims Please See Continuation Sheet NO

2. Citations and explanations:

Claims 8, 10-15, 17-18, 20, 23, 25, 27-51, 53-54, 56 and 58-76 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest the specific antibodies deposited with the ATCC having accession numbers PTA-5878, PTA-5879, PTA-6146, PTA-6147 and PTA-6629

Claims 1-7, 9, 16, 19, 21-22, 24, 26, 52, 55 and 57 lack novelty under PCT Article 33(2) as being anticipated by Keolsch et al (WO 98/22597, 28 May 1998).

Keolsch et al teach antibodies that bind napsin A, which as evidenced by the specification at page 11, lines 23-24 is identical to Lng105. The chemical structure (i.e., amino acid sequence) of the epitopes bound by the antibodies having ATCC accession numbers PTA-5878, PTA-5879, PTA-6146, PTA-6147 and PTA-6629 are indefinite because the instant application does not identify the chemical structure of these epitopes. Therefore, it is the examiner's position that the antibodies of Keolsch et al, particularly the polyclonal antibodies would compete for the same epitopes recognized by the antibodies having ATCC accession numbers PTA-5878, PTA-5879, PTA-6146, PTA-6147 and PTA-6629. One of ordinary skill in the art would reasonably conclude that Keolsch et al antibodies also possesses the same structural and functional properties as those of the antibodies claimed and, therefore, it appears that Keolsch et al have produced antibodies that are identical to the claimed antibodies. Since the Patent and Trademark Office does not have the facilities for examining and comparing the claimed antibodies with the antibodies of Keolsch et al, the burden of proof is upon the Applicants to show an unobvious distinction between the structural and functional characteristics of the claimed antibodies and the antibodies of the prior art. See *In re Best*, 562 F.2d 1252, 195 U.S.P.Q. 430 (CCPA 197) and *Ex parte Gray*, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.).

Keolsch et al teach monoclonal antibodies, humanized antibodies, single-chain antibodies, and labeled antibodies and Keolsch et al teach a method of detecting napsin A comprising contacting human kidney 293 cells and determining the level of binding (see pages 8-9, 11-13 and 15). Claim 26 is drafted in the product-by-process format. The recitation of a process limitation in claim 26 is not viewed as positively limiting the claimed product absent a showing that the process of making recited in claim 26 imparts a novel or unexpected property to the claimed product, as it is assumed that equivalent products are obtainable by multiple routes. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. *In re Thorpe*, 227 USPQ 964, 966 (Fed. Cir. 1985). See also MPEP 2113.

Claims 1-76 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.

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International application No.
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Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

V.1. Reasoned Statements:

The opinion as to Novelty was positive (Yes) with respect to claims 8, 10-15, 17-18, 20, 23, 25, 27-51, 53-54, 56, 58-76

The opinion as to Novelty was negative (No) with respect to claims 1-7, 9, 16, 19, 21-22, 24, 26, 52, 55, 57

The opinion as to Inventive Step was positive (Yes) with respect to claims 8, 10-15, 17-18, 20, 23, 25, 27-51, 53-54, 56, 58-76

The opinion as to Inventive Step was negative (NO) with respect to claims 1-7, 9, 16, 19, 21-22, 24, 26, 52, 55, 57

The opinion as to Industrial Applicability was positive (YES) with respect to claims 1-76

The opinion as to Industrial Applicability was negative (NO) with respect to claims NONE

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Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the questions whether the claims are fully supported by the description, are made:

Claims 1-19 are objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 6 because claims 1-19 indefinite for the following reason(s): the instant application does not characterize the epitopes that are recognized by the antibodies deposited as ATCC accession numbers PTA-5878, PTA-5879, PTA-6146, PTA-6147 and PTA-6629. Thus, the metes and bounds of the epitopes recognized by these antibodies are unclear.